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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/764,985

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Masanori Terajima

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EXAMINER

LI, BAO Q

ART UNIT

PAPER NUMBER

1648

DATE MAILED: 05/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/764,985

Applicant(s)

TERAJIMA ET AL.

Examiner

Bao Qun Li

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 March 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) 1-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>Nov. 18, 05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This is to acknowledge the amendment filed on March 23, 2006. Claims 19, 21, 24, 28 and 33 have been amended. Claims 1-34 are pending.

Election/Restrictions

1. Applicant's election of group III, claims 19-34 in the scope of SEQ ID NO: 2 in the reply filed on March 23, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Claims 1-18 are withdrawn from the consideration.
3. Claims 19-34 in the scope of SEQ ID NO: 2 are considered. Applicants are reminded to amend claims to the elected scope for reflecting the examination on the record.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.
5. Claims 19-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
6. Claims 19-34 are vague and indefinite in that the metes and bounds of "an immunogenic mutant or fragment thereof" are not defined in the indefinite claims 19, 24 and 29. The claimed is interpreted in light of the specification; however, the specification does not give a clear definitions about what the cited "immunogenic mutant" or "fragment thereof" are defined. Therefore, the claims are considered indefinite.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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8. Claims 19-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using the specific smallpox virus epitope of SEQ ID NO: 2 to stimulate the T cells that are previously exposed with said smallpox virus, does not enable for using said peptide to activate any population of T cells that previously exposed to any or all vaccinia virus or variola virus or their vaccine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

9. Moreover, the claims 19-34 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using the specific smallpox virus peptide of SEQ ID NO: 2 to stimulate the T cells that are previously exposed to said smallpox virus, does not enable for using any antigenic mutant or fragment thereof to activate any population of T cells given they are previously exposed to any or all vaccinia virus or variola virus or a vaccine thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

10. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would render undue experimentation (See *United States v. The Krypton Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). These factors include the following: (1). Nature of Invention, (2). Scope of the invention, (3). State of art, (4). Unpredictability in the field, (5). Number of working example, (6). Amount of guidance presented in the specification, and (7). Level of skill in the art.

11. The nature of the invention is directed to a method for activating a population of T cells with a smallpox HLA-A0201 epitope containing peptide against the same smallpox virus, wherein the population of T cells may be previously exposed to said small pox virus. However, the broad scope of the claims read on using any mutant or fragment of peptide of SEQ ID NO:2

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thereof to activate a population of T cells previously exposed to any kinds of vaccinia virus. The broad reasonable interpretation of a mutant or a fragment of peptide of SEQ ID NO: 2 can read as small as a peptide containing only one or two amino acid residues derived from the SEQ ID NO: 2.

12. It is well known in the art that poxviridae is a large family of DNA viruses, but they do not cross-react each other. For example, the antigens of smallpox virus does not cross-react with that of other poxvirus, such as the immune response produced by the chicken pox virus. Therefore, it is unpredictable whether said smallpox peptide of SEQ ID NO: 2 can stimulate any or all T cells that are previously exposed to any or all vaccinia viruses.

13. Moreover, it is also well known in the art that a biological function of a protein really depends on the integrity of certain critical part of a protein. An amino acid substitution for a ligand may lead to change the specificity of ligand-receptor interactions either by changing the physiochemical properties of side chains or by altering residues in the core of the ligand leading to a change in surface shape as evidenced by Skelton et al. (Biochemistry 1995, Vol. 34, pp. 5329-5342. Please see lines 28-33 on the 2nd col. of page 5339). This functional and structural relationship is a universal phenomenon for any biologically active molecule. Even a single mutation in the amino acid sequence can lose the original biological function of said protein as evidenced by Lazar (Molecular and Cellular Biology 1988, Vol. 8, No. 3, pp. 1247-1252. See entire document), and Smilek et al. (Proc. Natl. Acad. Sci. USA, 1991, Vol. 88, pp. 9633-9637, see abstract).

14. Therefore, it is very unpredictable whether the biological effect of any mutant or fragment of SEQ ID NO: 2 will have the same biological activity as claims 19-34 required.

15. The specification only teaches to use peptide of SEQ ID NO: 2 to activate the smallpox pre-exposed cells. The specification does not teach how to select or produce said mutant or fragment of SEQ ID NO: 2. The specification does not teach that said peptide is able to activate any or all vaccinia virus pre-exposed T cells. Therefore, the specification fails to provide sufficient evidence to support the broad scope of claimed invention.

16. Given the above analysis of the factors which the courts have determined are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan

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would have to conduct undue and excessive experimentation in order to practice the claimed invention.

Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

18. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

19. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b). An obvious-type double patenting rejection is appropriate where the conflict claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. *Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887,225 USPQ 645 (fed. Cir. 1985).

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20. Claims 19-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 28-43 over copending Application No. 11,238,122. Although the conflicting claims are not identical, they are not patentably distinct from each other because the conflict claims have overlapping scopes and they are obvious version each form other.

21. In the instant case, the claims of current application claims to use one of the peptide 165, i.e. SEQ ID NO: 2 to stimulate T cells and observe the T cells activations, wherein the method is selected from ELISAPOT, or cytometry assay. The conflict claims in application No. 11,238,122 also claim to a method of using a peptide including the peptide 165. Therefore, the scope of the claims 19-34 in the current application is overlapped with that of claims 28-43 of the copending application. Therefore, they are anticipated each from other.

22. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

23. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

24. Claims 19-34 are rejected under 35 U.S.C. 102(a) as being anticipated by Drexler et al (PNAS January 2003, Vol. 100, No. 1, pp. 217-222).

25. The broad scope of the claimed invention can be reasonable interpreted as a method of activation of a population of T cells in the presence of a previous vaccinia virus or variola virus infection or vaccination. The method comprises to administer a HLA-A 0201 restricted T cell epitope containing peptide i.e. peptide 165 designated as SEQ ID NO: 2 or any mutant or fragment thereof to a population of T cells in the presence of vaccinia or variola virus, wherein the T cells is harvested from a blood, preferably peripheral mononuclear cells, a lymph and a tissue. The method for measuring the activation consists of a cytokine assay, and the flow cytometry assay.

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26. Drexler et al. teach a method for activating a population of T cells isolated from the vaccinia virus immunized mouse using a HLA-A 0.021 –restricted T cell epitope containing peptide. The method comprises to immunize the mice with the virus or virus derived peptide and later test the activation of the T cells isolated from the blood or spleen cells of said animals with a HLA-A 0201 restricted T cell epitope containing peptide. Because the claimed mutant does not have any structural limitation, all disclosed peptides used by the prior art can be considered as mutants of the claimed peptide 165 since they all contain one or more amino acid residues of peptide of SEQ ID NO: 2, and they are also characterized to be a HLA-A 0201 restricted T cell epitope that exhibit similar functions, such as cytokine INF- γ and TNF- α productions measured by staining the cells with FITC labeled antibodies followed by the flow cytometry (See Fig. 1, abstract and page 218). Therefore, the claimed invention is anticipated by the cited reference.

27. Claims 19-34 are rejected under 35 U.S.C. 102(a) as being anticipated by Drexler et al (EP 1, 398,380A1).

28. The broad scope of the claimed invention can be reasonably interpreted as a method of activation of a population of T cells in the presence of a previous vaccinia virus or variola virus infection or vaccination. The method comprises to administer a HLA-A 0201 restricted T cell epitope, i.e. peptide 165 designated as SEQ ID NO: 2 or any mutant or fragment thereof to a population of T cells in the presence of vaccinia or variola virus, wherein the sample used for getting the T cells is selected from the group consisting of blood, preferably peripheral mononuclear cells, lymph and tissue, and the method for measuring the activation consists of a cytokine assay, preferably ELISPOT assay, and the flow cytometry assay.

29. Drexler et al. teach a method for detecting a T cell response induced by smallpox vaccines in human comprising to contacting a sample containing T cells from a patient has been immunized with a smallpox vaccine or orthopoxvirus vector vaccine, and co-culturing said sample with one or more peptides that contain HLA-A 0201 restricted T cell epitope, which is considered as variant or mutant of the claimed peptide 165 since they all contain one or more amino acid residues of claimed peptide of SEQ ID NO: 2, and they are also characterized as a HLA-A 0201 restricted T cell epitope (See SEQ ID NOS 1-50, pages 23-24 and paragraph

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[0078]). The T cells activations were measured with cytokine INF- γ and TNF- α productions as well as CD8+ T cell activations done by ELISPOT, intracellular cytokine staining followed by flow cytometry etc. The T cells are harvested from a human body fluid, preferably a blood sample (See claims 22-28) or the assay were done in animals preimmunized with a vaccinia vaccine (See paragraph [0070-0077 and Figs. 2-3).

30. Because the claimed mutant does not have any structural limitation, all disclosed peptides used by the prior art can be considered as mutants of the claimed peptide 165 since they are all contains one or more amino acid residues of peptide of SEQ ID NO: 2, and they are also characterized to be a HLA-A 0201 restricted T cell epitope exhibiting similar functions (See paragraph [0065-0069]. Therefore, the claimed invention is anticipated by the cited reference.

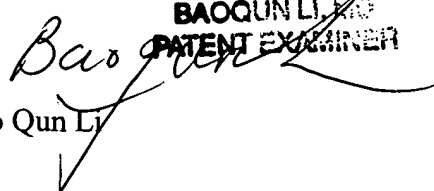
Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


BAOQUN LI, ESQ.
PATENT EXAMINER
Bao Qun Li